

**REMARKS**

Claims 35, 39, 41, 42, 46 and 48 are all the claims pending in the application.

**A) Claim Rejections - 35 U.S.C. § 103**

Claims 35, 39, 42 and 46 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Beemsterboer, et al., U.S. Patent No. 4,145,345. According to the Examiner, the reference teaches a process of separating maytansine from other maytansinoid components using chromatography (see column 1, lines 40-55 and also column 3, line 55 to column 4, line 9). The Examiner stated that the claims differ by requiring that maytansinol rather than a maytansine is isolated. However, the Examiner asserted that one skilled in the art would be motivated to isolate any maytansinoid using chromatography, because the reference teaches isolation of maytansine from other maytansinoid components using chromatography.

For the following reasons, the rejection is traversed, respectfully.

Applicants first are struck by the broad statement by the Examiner (see office action page 2, large paragraph, line 2) that the reference teaches a process of separating maytansine from other maytansinoid components using chromatography, and that the claims differ by requiring that maytansinol is to be isolated. Neither the Beemsterboer patent nor the present application claims refer to chromatography in this broad sense. Chromatography is a separation process described in Webster's dictionary as "a process in which a chemical mixture carried by a liquid or gas is separated into components as a result of differential distribution of the solutes as they flow around or over a stationary liquid or solid phase." Such chromatographic processes are performed using many different methods. It is such methods that are the subject of the Beemsterboer patent and the present application.

To achieve the separation of a certain component from a mixture, often one can not apply generally known chromatographic methods. Rather, one has to develop or invent one's own method. Such methods are quite specific for the separation task. The most important elements for a chromatography method are the mobile and stationary phases. Gas chromatography uses a gas as the mobile phase, liquid chromatography uses a liquid solvent or a mixture of liquid solvents as the mobile phase. Beemsterboer and the present process claims use liquid chromatography methods. There are many different types of stationary phases for liquid chromatography, such as alumina, silica gel, charcoal powder or beads, chemically modified silica gel, synthetic polymers that in addition can carry different types of charged ligands, natural polymers such as cellulose and agarose, chemically modified natural polymers, etc.

Thus, both the separation task and the chromatographic separation methods must be considered when applying the teachings of the reference to the claims.

As described below, the separation task and the chromatographic separation methods disclosed in the Beemsterboer patent and claimed in the present application are entirely different.

Beemsterboer teaches a method of isolating maytansine from an ethanolic solution that contains the extract from woody plants. The method of isolation uses a chromatographic process wherein the stationary phase is silica gel and the mobile phase is methylene chloride containing increasing amounts of more polar solvents. As mentioned above, typically such new methods have to be invented for the isolation of a certain compound from a certain mixture. Here it is maytansine from a plant extract. This extract contains a myriad of compounds and maytansinoids constitute only a small percentage. Starting with 15.5 g of extract (column 6, line 21), 2.1089 g of substantially pure maytansine was obtained (column 6, line 34). This was

subjected to a second chromatography (column 6, line 66) to yield 1.262 g of pure maytansine (column 7, line 5), which is 8.14% of the starting extract.

The present application claims a novel method of isolating maytansinol from a mixture of unreduced and over-reduced maytansinoids. Thus the task is a more difficult one - the process isolates one maytansinoid, which is maytansinol, from other maytansinoids. In other words, the presently claimed process separates one member of a group of chemically very similar compounds, which all belong to the class of compounds, called maytansinoids. Beemsterboer isolates one compound, which is maytansine, from a plant extract. Such extracts typically contain many different chemical compounds that are chemically very diverse and, therefore, are easier to separate. The presently claimed process uses a chromatographic process wherein the stationary phase is chemically modified silica gel (*e.g.* cyano-bonded silica) and the liquid phase is an organic solvent, because the chromatography is performed "by normal phase HPLC."

Furthermore, the presently claimed process uses HPLC, whereas Beemsterboer uses regular silica gel column chromatography. Typically, easier separation problems are solved by regular silica chromatography, more challenging problems are solved by high-performance liquid chromatography (HPLC).

Thus, there are no similarities between the process of the Beemsterboer patent and the presently claimed process. Accordingly, the Beemsterboer patent in no way teaches or suggests the presently claimed process.

In view of the above, the Examiner is requested to reconsider and remove this rejection.

**B) Claim Rejections - 35 U.S.C. § 102**

Claims 37, 38, 41 and 48 were rejected under 35 U.S.C. § 102(b) as being anticipated by Chari, et al., U.S. Patent No. 5,208,020. The Examiner stated that the '020 patent teaches cell-binding agent maytansinoid complexes (see Example 3).

Claims 37 and 38 have been canceled. Thus, the rejection is moot as to these claims.

With respect to claims 41 and 48, the rejection is traversed, respectfully. Specifically, both claims 41 and 48 are process claims, and their patentability depends upon the process not upon the product that is made. Further, claim 41 depends from process claim 35 and claim 48 depends from process claim 42. Accordingly, since both claims 35 and 42 are patentable, claims 41 and 48 should also be considered patentable.

In view of the above remarks and cancellation of claim 37 and 38, the Examiner is requested to reconsider and remove this rejection.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

SUGHRUE MION, PLLC  
Telephone: (202) 293-7060  
Facsimile: (202) 293-7860

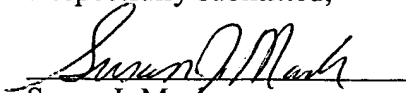
WASHINGTON OFFICE

**23373**

CUSTOMER NUMBER

Date: May 2, 2005

Respectfully submitted,

  
Susan J. Mack  
Registration No. 30,951